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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,332	07/23/2004	Marie Malissen	BJS-3665-113	9194

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EXAMINER	
TON, THAIAN N	
ART UNIT	**PAPER NUMBER**
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,332	MALISSEN ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,37,38,43,44 and 46-64* is/are pending in the application.

4a) Of the above claim(s) *38,48-56 and 62-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35, 37, 43, 44, 46,47, 57-61 v* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/17/07 has been entered.

The After-Final Amendment, filed 6/20/07, has been entered. Claims 35, 37, 38, 43, 44, 46-64 are pending; claims 1-34, 36, 39-42 and 45 are cancelled; claims 38, 48-56, 62-64 are withdrawn; claims 35, 37, 43, 44, 46,47, 57-61 are under current examination.

Applicants did not file Remarks with the 7/17/07 submission, therefore, the Examiner addresses Applicants' Remarks After Final (filed 6/20/07) as they pertain to the rejections of record.

The Malissen Declaration, filed 6/20/07, has been considered.

Election/Restrictions

Claims 38, 48-56, 62-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/22/06.

Claim Objections

The prior objection to claim 47 is rendered moot in view of Applicants' amendments to the claims, no longer reciting the term "rodent".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35, 37, 41-44, 46, 47, 57-61 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

1. A transgenic mouse **whose genome** comprises a mutant mouse LAT gene encoding a mutant mouse LAT protein wherein the sequence of the mutant LAT protein comprises a single mutation of a tyrosine located at position 136 of the wild-type mouse LAT protein sequence, wherein the mutation is not a composite mutation of the tyrosine residues at positions 176, 195 and 235 of said wild-type mouse LAT protein sequence, wherein the single mutation of the tyrosine located at position 136 consists of a replacement with a reside that prevents the association with the SH2 domain of proteins, wherein the mouse is homozygous for said mutated mouse LAT protein, wherein the mouse has a phenotype of exaggerated TH2 cell differentiation, or

2. A transgenic mouse **whose genome** comprises one allele for a mutant mouse LAT gene encoding a mutant mouse LAT protein wherein the sequence of the mutant LAT protein comprises a single mutation of a tyrosine located at position 136 of the wild-type mouse LAT protein sequence, wherein the mutation is not a composite mutation of the tyrosine residues at positions 176, 195 and 235 of said wild-type mouse LAT protein sequence, wherein the single mutation of the tyrosine located at position 136 consists of a replacement with a reside that prevents the association with the SH2 domain of proteins, and is a carrier of a null allele of the LAT gene, wherein the mouse has a phenotype of exaggerated TH2 cell differentiation,

3. A mutant mouse LAT gene encoding a mutant mouse LAT protein wherein the sequence **of the mutant LAT protein** comprises a single mutation of a

tyrosine located at position 136 of the wild-type mouse LAT protein sequence, wherein the mutation is not a composite mutation of the tyrosine residues at positions 176, 195 and 235 of said wild-type mouse LAT protein sequence, wherein the single mutation of the tyrosine located at position 136 consists of a replacement with a reside that prevents the association with the SH2 domain of proteins,

4. Cells isolated from the transgenic mouse of #1 or #2.

The specification does not reasonably provide enablement for the breadth of the claims, which encompass chimeric mice, non-genome integrated transgenic mice, cells isolated from said mice. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Applicants' Arguments are found to be persuasive with regard to these aspects of the prior rejection:

1. Applicants' Amendment to the claims, which now recites a mouse, overcomes the prior rejection, with regard to the unpredictability in phenotype. See pages 5-6 of the prior Office action.

2. Applicants' Amendment, which now requires that the tyrosine at position 136 be replaced by a residue preventing the association with the SH2 domain of proteins, overcomes the prior rejection with regard to the unpredictability in residue mutation. See pages 7-8 of the prior Office action.

3. The Malissen Declaration overcomes the prior rejection of record, with regard to the phenotype of a mouse which carries a null allele of the LAT gene,

because the Declaration shows that knockout LAT mice have the same phenotype as mice that have the Y136F mutation.

The claimed invention is not fully enabled because it does not recite that the mutation is genome integrated. In particular, claim 35 recites a mouse having a mutated LAT gene, this mouse could have a single copy of the mutated gene, in a single cell, or the mouse could be a chimeric, where some (but not all) of its cells contain the mutated LAT gene. In fact, claim 46 further limits the mouse by stating that the mutated LAT gene is incorporated into the mouse genome by targeted insertion. Additionally, the broad claims encompass mice that have a mutated LAT gene that is not under the regulatory controls of the endogenous LAT gene, and thus, would appear to have a mutated LAT gene, that could be randomly inserted, as well as the endogenous LAT gene. The instant specification fails to enable the chimeric mice, or mice that comprise a non-genome integrated mutant LAT gene (as instantly claimed). The specification fails to teach the phenotype of any these mice, and thus, one of skill in the art, in view of the unpredictability of the resultant phenotype (see prior Office actions), would have to practice undue experimentation to make and use these mice. Additionally, claim 47, which recites cells isolated from the mouse of claim 35 or progeny of this mouse, fail to be enabled, because the mouse of claim 35 encompasses chimeric mice (see above), cells from this mouse could be wild-type cells that do not have the mutated LAT gene; similarly, progeny of these mice could be wild-type mice, if the mouse fails to have germ-line transmission of the mutated LAT gene. Applicants have provided no enabled uses for wild-type cells or mice in the context of the claimed invention. It is suggested that Applicants amend the claims to recite that the mutant LAT gene is integrated into the mouse's genome, as indicated in the scope of enablement.

Accordingly, in view of the state of the art, with regard to the unpredictability in phenotype of knockout mice, the breadth of the claims, which

encompass chimeric mice and mice with non-genome integrated mutated LAT genes, the lack of guidance or teachings provided by the specification with regard to the resultant phenotype of any of the mice, other than that which has been provided as the enabled scope, it would have required undue experimentation for one of skill in the art to make and use the claimed invention.

Written Description

The prior rejection of claims 35, 37, 41-44, 46, 47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amendment to the claims does not overcome the prior rejection of record, because it states that the sequence of the mutant LAT protein differs from a mouse wild type sequence by a single mutation of a tyrosine located at position 136 of the wild-type mouse LAT protein sequence.

The specification provides guidance for a mutant mouse LAT gene encoding a mutant mouse LAT protein wherein the sequence of the mutant LAT protein comprises a single mutation of a tyrosine located at position 136 of the wild-type mouse LAT protein sequence, wherein the mutation is not a composite mutation of the tyrosine residues at positions 176, 195 and 235 of said wild-type mouse LAT protein sequence, wherein the single mutation of the tyrosine located at position 136 consists of a replacement with a reside that prevents the association with the SH2 domain of proteins. The specification does not provide guidance for the claimed invention, because the claims recite that the mutant LAT protein only differs from "a mouse wild type sequence". This language does not require a comparison between the mutant mouse LAT sequence and the endogenous mouse

LAT sequence, as it encompasses mutants that only differ from any wild-type mouse sequence that has a tyrosine at the 136 position of the wild-type mouse LAT protein sequence. It is suggested that Applicants amend the claims to language that clearly shows that the mutant LAT protein sequence differs from the wild-type mouse LAT sequence at position 136, for example, by stating that the sequence of the mutant LAT protein comprises a single mutation of a tyrosine located at position 136 of the wild-type mouse LAT protein sequence, as indicated above, to obviate this rejection.

Accordingly, the prior rejection of record is maintained.

Claim Rejections - 35 USC § 112

The prior rejection of claim 41, under 112, 2nd paragraph, is rendered moot in view of Applicants' cancellation of the claim.

The prior rejection of claim 37, under 112, 2nd paragraph, is withdrawn in view of Applicants' Amendment to the claim, which now depends from claim 35.

The prior rejection of claim 47, under 112, 2nd paragraph, is withdrawn in view of Applicants' amendment to the claim,

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35, 37, 43, 44, 46, 47, 57-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of claim 35 remain unclear. The claim now recites that the sequence of the mutated LAT protein differ from a "mouse wild-type sequence". This encompasses any mouse wild-type sequence. It is suggested that Applicants amend the claim to recite language that it is the wild-type mouse LAT

sequence that the mutated LAT sequence is compared to. Therefore, this rejection is maintained.

Claim 37 is unclear. The metes and bounds of the claim cannot be determined, because the claim recites that the "mutated LAT gene coding for a mutant LAT protein comprises exon 7 of the mutated gene (SEQ ID NO: 2)." SEQ ID NO: 2 is a nucleic acid sequence; additionally, proteins do not contain exons, nucleic acid sequences contain introns and exons. Appropriate correction is required.

The metes and bounds of claim 57 is unclear, because the claim recites, "the sequence of which differs" (see line 2). It is unclear if "the sequence" refers to the LAT protein or nucleic acid sequence. It is suggested that the claim recite, "the sequence of the mutant LAT protein." Claims 58-61 depend from claim 57.

Claim Rejections - 35 USC § 102

The prior rejection of claims 47 and 57-61 under 35 U.S.C. 102(a) as being anticipated by Sommers *et al.* is withdrawn in view of Applicants' Amendment to the claims, which now recites that the mutation is not a composite mutation of the tyrosine residues at positions 175, 195 and 235 of the wild-type mouse LAT protein sequence.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Peter Paras, SPE of Art Unit 1632, at (571) 272-4517. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Thaian N. Ton/
Primary Examiner
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